

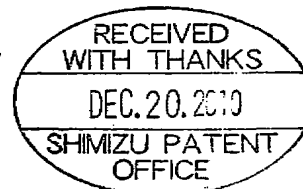
From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44bis.3(c) and 72.2)

To:

SHIMIZU, Hatsushi
Kantetsu Tsukuba Bldg. 6F
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JAPON



Date of mailing (day/month/year) 09 December 2010 (09.12.2010)	
Applicant's or agent's file reference C1-A0801Y2P	IMPORTANT NOTIFICATION
International application No. PCT/JP2009/057309	International filing date (day/month/year) 10 April 2009 (10.04.2009)
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA et al	

1. Transmittal of the translation to the applicant.



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

EP

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AO, AP, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Gijsbertus Beijer

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference C1-A0801Y2P	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2009/057309	International filing date (<i>day/month/year</i>) 10 April 2009 (10.04.2009)	Priority date (<i>day/month/year</i>) 11 April 2008 (11.04.2008)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 30 November 2010 (30.11.2010) Authorized officer <p style="text-align: center; font-weight: bold;">Gijsbertus Beijer</p> e-mail: pt07.pct@wipo.int
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PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing
(day/month/year)

Applicant's or agent's file reference

C1-A0801Y2P

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/JP2009/057309

International filing date (day/month/year)

10.04.2009

Priority date (day/month/year)

11.04.2008

International Patent Classification (IPC) or both national classification and IPC

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP

Date of completion of this opinion

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2009/057309

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ on paper
 - ☒ in electronic form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in electronic form
 - ☐ furnished subsequently to this Authority for the purposes of search
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2009/057309

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:

The inventions in claims 1-50 include three inventions: an invention set forth in claims 1 and 9-14 relating to an antigen-binding molecule lower in binding activity at pH 5.8 than at pH 7.4; an invention set forth in claims 18-23 relating to a method including having amino acid of an antigen-binding molecule substituted for or inserted into histidine; and an invention set forth in claims 28, 30-32 and 43-46 relating to a method of screening or manufacturing an antigen-binding molecule higher in binding activity at a first pH than at a second pH.

Further, a method of producing an antibody having reduced binding to an antigen under acid conditions by introducing at least a histidine residue is publicly known (see FEBS Lett., 1992, vol. 309, no. 1, pages 85 to 88, if necessary). Therefore, these three inventions do not share a special technical feature, and are not considered to be so linked as to form a single general inventive concept.

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☒ all parts
 - ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2009/057309

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-50	YES
	Claims		NO
Inventive step (IS)	Claims	9-27	YES
	Claims	1-8, 28-50	NO
Industrial applicability (IA)	Claims	1-50	YES
	Claims		NO

2. Citations and explanations:

Document 1: FEBS Lett., 1992, vol. 309, no. 1, pages 85 to 88

Claims 1-8 and 28-50

The invention as in claims 1-8 and 28-50 does not involve an inventive step in view of document 1 cited in the ISR.

Document 1 discloses a method of producing an antibody having reduced binding to an antigen under acid conditions by introducing histidine into a CDR region of an antibody. The antibody obtained by the method is considered to be lower in binding activity under a condition of pH 5.2 than under a condition of pH 7.8.

Accordingly, a person skilled in the art could easily produce, on the basis of the invention described in document 1, an antibody having reduced binding to an antigen under acid conditions by introducing histidine into a CDR region of an antibody, and there is no particular technical difficulty in setting the dissociation constant (KD) ratio to a desired value in such a manner that the binding activity is lower under a condition of pH 5.8 than under a condition of pH 7.4. Further, the obtained antibody is indistinguishable from the

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2009/057309

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

antigen-binding molecule in claims 1-7. Further, a special technical feature cannot be found in applying the obtained antibody for medicinal use.

Furthermore, in the invention described in document 1, a person skilled in the art could also have screened or produced, as required when necessary, an antibody having reduced binding to an antigen under acid conditions by introducing histidine into a CDR region of an antibody.

Claims 9-27

The invention as in claims 9-27 involves an inventive step in view of document 1 cited in the ISR.

Document 1 neither describes nor suggests the method set forth in claims 9-14 and 18-23 of the present application, which improves an antigen-binding molecule. Further, a person skilled in the art could not easily conceive of the feature.